



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PU4687WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/US 03/22716	International filing date (day/month/year) 21.07.2003	Priority date (day/month/year) 23.07.2002
International Patent Classification (IPC) or both national classification and IPC C07D487/04		
Applicant SMITHKLINE BEECHAM CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 04.02.2004	Date of completion of this report 28.07.2004
Name and mailing address of the International preliminary examining authority:  European Patent Office - Glitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Hoepfner, W Telephone No. +49 30 25901-337 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/US 03/22716**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*

Description, Pages

1-285 as originally filed

Claims, Numbers

1-34 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US 03/22716

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 18-26,28,29 (with respect to industrial applicability)
because:
- ☒ the said international application, or the said claims Nos. 18-26,28,29 relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.
- ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-34
	No: Claims	
Inventive step (IS)	Yes: Claims	1-34
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-17,27,30-34
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 18-26, 28 and 29 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, the International Examination Authority fully concurs with the objection put forward by the International Search Authority and no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: EP-A-1040831
D2: WO-A-02055082
D3: WO-A-0119829
D3: WO-A-02050065

Novelty

The document D1 discloses pyrazolopyrimidines and their use in the treatment of "sudden death" in diabetic patients, wherein the said pyrazolopyrimidines differ from the compounds of claim 1 in that they lack the particular hydrazone substituent at position 4 (see page 2, lines 54, 55; page 3, formula II).

The document D2 discloses pyrazolopyrimidines and their use in the treatment of neurological diseases such as Parkinson's disease, depression or pain, wherein the said pyrazolopyrimidines differ from the compounds of claim 1 in that they have substituents being completely different when compared to the compounds of claim 1 (see page 1, lines 9, 14, 15; page 6, formula (I); page 18, lines 30-33; pages 28-34, Table 1).

The document D3 discloses pyrazolopyrimidines as inhibitors for protein kinases such as TIE-2 and their use in the treatment of (amongst others) a "diabetic condition", wherein, again, the said pyrazolopyrimidines differ from the compounds of claim 1 in that they have substituents other than the compounds of claim 1 (see page 14, formula I; page 44, line 14; page 45, line 15; page 46, lines 8, 9).

Lastly, the document D4 discloses a variety of GSK-3 inhibitors and their use in the treatment of diabetes. Even if some of the D4 compounds have a pyrazolopyrimidine partial structure, they structurally vastly differ from the compounds of claim 1 (see page 6, formula I; page 20, line 10; page 201, partial structure IVd-V).

Consequently, in view of these documents novelty has to be acknowledged for the subject-matter of the independent claims 1, 16, 18, 23 and 26-30 and the dependent claims 2-15, 17, 19-22, 24 and 15.

Inventive step

D3 is regarded as the closest prior art for the novel subject-matter, since it addresses a similar problem, namely the provision of TIE-2 inhibitors useful in the treatment of diabetes, and since its compounds come in total structurally closer to the compounds of claim 1.

The distinguishing feature between the compounds of claim 1 and D1 is to be seen as the particular kind of substituents, namely an acyclic substituent at position 1 in combination with a heterocyclic group at position 3 and a nitrogen-containing group other than a hydrazone at position 4.

In the absence of any evidence for an unexpected technical effect linked to this feature, the objective problem solved by the novel subject-matter has to be regarded as the provision of further compounds useful in the treatment of diabetes.

However, notwithstanding this and even in the absence of a technical effect, the presence of inventive activity has to be acknowledged for the claimed solution to this very general problem, since the said solution, namely the provision of the particular compounds of claim 1, was not derivable from the prior art, neither alone nor in combination.

Industrial applicability

There is no doubt that the subject-matter of the present claims 1-17, 27 and 30-34 is industrially applicable.

However, for the assessment of the present claims 18-26, 28 and 29 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US 03/22716

to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Formal matters, clarity

Although in the present claims terms such as "alkyl", "alkylsulfonyl", "alkoxy", "aryl" and the like (see e.g. claim 1) are clear as such, they introduce obscurity in that they unduly extend the scope of the claimed subject-matter (breadth of the claims).

In the present independent claim 30, language such as "with reference to any of the Examples" introduces obscurity and thus renders the claim unclear within the meaning of Art. 6 PCT, since it refers to the whole content of the experimental data. Moreover, such language interferes with Rule 6.2 a) PCT.